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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
10/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/564,096	LIZIO ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 35* is/are pending in the application.

4a) Of the above claim(s) *2, 5, 12 - 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 6 - 11, 33 - 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed July 30, 2008, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 3, 4, and 6 – 11 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 5 and 17 – 19 of copending Application No. 12/030377. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 30, 2008.

Applicant has requested that this rejection be held in abeyance until otherwise allowable subject matter has been identified in this application.

Claim Rejections - 35 USC § 112 – 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 10 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. A new matter rejection was made over the mixture of active ingredients as recited as the last element in the Markush group of this claim. Applicant traverses this rejection on the basis that claim 10 is an original claim and the concept of incorporating active substances is described in the specification.

This rejection is WITHDRAWN as an amendment to claim 10, adding "and mixtures thereof" was filed on the filing date of the instant application. However, as there was no support found for this concept in the international stage application, the priority date for claim 10 is the actual U.S. filing date of May 2, 2006.

5. Claims 1, 3, 4, and 6 – 11 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 30, 2008 and those set forth below.

Applicant traverses this rejection on the basis that this is an original claim, no rejection of the elected species for lack of adequate description has been made and that as generically claimed, they from a well known structural feature that would be recognized by those of skill in the art.

These arguments are not found to be persuasive. These claims were rejected under the written description provision as lacking sufficient support for the genus of "protein derivatives and conjugates". The specification provides insufficient written description to support the genus of protein derivatives or conjugates encompassed by the claim, since there is no description of the structural relationship of these derivatives provided in the specification and Applicant has not provided a description as to how the base molecule may be changed while remaining a derivative. For example, proteins are broken down into individual amino acids during digestion, and Applicant has not indicated whether these individual amino acids or products made from those individual amino acids would or would not be considered part of the genus of "protein derivatives or conjugates".

6. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant have added new claim 33, in which gelatin is excluded from the composition and has cited the examples in which no gelatin

is present as support for this claim. The failure of a composition provided in the specification to include a certain ingredient not explicitly mentioned is not sufficient to support this new the exclusion of that particular ingredient from the composition. Therefore, the limitation of a composition that does not contain gelatin does have support in the manner required by 35 USC 112 ¶ 1.

7. Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant have added new claim 33, in which the particles do not possess a layer separating the inner matrix and outer coating. The failure of a composition to have such a layer is not sufficient to support the new limitation excluding such a layer. Therefore, the limitation of a composition that does not contain a layer separating the inner matrix and outer coating does have support in the manner required by 35 USC 112 ¶ 1. It is noted that the additional advantages conferred by the embedding of the active ingredient in a lipophilic matrix material is discussed, beginning at ¶ [0132] of the PGPub of the instant specification. As this ingredient is discussed as a component that may be included in the specification, the limitation of not having a mucoadhesive lipophilic matrix is supported by the originally filed disclosure.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim contains the broad limitation of a copolymer of 50 wt% methylmethacrylate and 50 wt% methacrylic acid, followed in parentheses by the trade name Eudragit® L. It is unclear whether the broad recitation of a 50:50 blend of these polymers is being claimed or a particular polymer blend form a particular source. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). Where a trademark or trade name is used in a claim as a

limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 3, 6 – 8, 10 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. (US 6,465,626). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 30, 2008 and those set forth. This is rejection is now applied to claims 1, 3, 6 – 8, 10, 11 and 34.

Applicant traverses this rejection on the basis that the present invention is directed to a mucoadhesive formulation such as chitosan whereas the compositions of Watts et al. contain significant amounts of gelatin, a bioadhesive compound, which exhibits a disadvantageous effect compared to the mucoadhesive ingredients of the instant invention. Reference is made to a further description of the binding of gelatin to the glycocalyx membrane and not the mucus membrane in WO 93/13753 is made. Watts et al. does not suggest the selection of a polymer with the mucoadhesive effect as required in the instant claims. The claims have also been amended to recite that the inner matrix layer consists essentially of a mucoadhesive polymer.

These arguments are not found to be persuasive.

The Examiner remains unclear as to the difference between "mucoadhesive" and "bioadhesive" as the document cited by Applicant, WO 93/13753 from which these citations appear to be from based on the total number of pages and its provided equivalent EP 0621775, are not in English. Definitions for "mucus", "mucin" and "glycocalyx" from Stedman's Medical Dictionary (2000) are attached. As both the glycocalyx and mucus contain glycoproteins, it appears to the Examiner that various polymers would bind in essentially the same manner to either the glycoproteins of the glycocalyx attached to a cell or to the glycoproteins of the mucin in the mucus layer not attached to cells.

Additionally, Applicant has not provided a definition as to what elements are excluded by the transitional phrase "consisting essentially of". The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. In re Herz, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original) "A consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). See also Atlas Powder v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984); In re Janakirama-Rao, 317 F.2d 951, 137 USPQ 893 (CCPA 1963); Water Technologies Corp. vs. Calco, Ltd., 850 F.2d 660, 7 USPQ2d 1097 (Fed. Cir. 1988). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear

indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) **MPEP 2111.03**

Therefore, the amendments to the claims have not excluded the gelatin containing compositions of Watts et al. from the claims and therefore this rejection is MAINTAINED.

Evidence indicating that the mucoadhesive limitations of the instant claims are not possessed by the compositions of Watts et al. would be sufficient to overcome this rejection. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

14. Claims 1 and 4 were rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. further in view of Berliner et al. (US 5,849,327). This rejection is

MAINTAINED for the reasons of record set forth in the Office Action mailed April 30, 2008 and those set forth below.

Applicants arguments with respect to Watts et al. have been discussed above. As Berliner et al. only teaches the coating thickness and not the mucoadhesive inner matrix, this rejections should be withdrawn.

This is not found to be persuasive. As discussed in greater detail above, the amendments to the claims are not sufficient to overcome the rejection of Watts et al. and therefore Berliner et al. need not teach a mucoadhesive inner matrix.

15. Claims 1, 9 and 10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. in view of Engel et al. (US 5,773,032). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed April 30, 2008 and those set forth below. This rejection is now applied to claims 1, 9, 10, 34 and 35.

Applicants' arguments with respect to Watts et al. have been discussed above. As Engel teaches the active ingredient cetrorelix but not the other elements of the invention such as the mucoadhesive inner matrix, this rejection should be withdrawn.

This is not found to be persuasive. As discussed in greater detail above, the amendments to the claims are not sufficient to overcome the rejection of Watts et al. and therefore Engel et al. need not teach a mucoadhesive inner matrix.

New Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Shimono et al. (EP 1203590).

Shimono et al. discloses a nonpareil that is coated the active ingredient, chitosan and EUGRAGIT® RS that are prepared in example 6 (col 12, ln 39 – 55). This layer is then coated with the 50% methlymethacrylate, 50% methacrylic acid EUDRAGIT® L to give a particle with a diameter of 1.4 mm (example 7, col 13, ln 1 – 11) and does not contain a layer separating the inner matrix and the outer coating. This outermost coating is an enteric polymer that meets the pH limitations of claim 34, as EUGRADIT® L is exemplified for the outer coating in dependent claim 35.

New Claim Rejections - 35 USC § 103

18. Claims 1 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimono et al. (EP 1203590) in view of Watts et al. (6,465,626).

Shimono et al. discloses a nonpareil that is coated with a layer comprising chitosan and EUGRAGIT® RS that are prepared in example 6 (col 12, ln 39 – 55) that

are further coated with the 50% methlymethacrylate, 50% methacrylic acid EUDRAGIT® L to give a particle with a diameter of 1.4 mm (example 7, col 13, ln 1 – 11).

Shimono et al. does not disclose the inclusion of cetrorelix as the active ingredient in the dosage from.

Watts et al. has been discussed in greater detail in the Office Action mailed April 30, 2008 and above, and discloses that compositions of bioadhesive matrices with enteric coatings can be used to prevent release of the therapeutic agent until it reaches the small intestine or colon (col 7, ln 10 – 36). Among the active ingredients which can be delivered using such a deliver system is LHRH (lutensing hormone release hormone) and analogs such as nafarelin, buserein, leuprolide and goserelin (col 6, ln 3 – 5). The peptide/protein active ingredients are embedded in the chitosan/gelatin matrix for delivery to the small intestine or colon.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare the sustained release dosage form comprising an inner chitosan containing layer with an enteric coating layer utilizing a methacrylic acid/methacrylate polymer such as EUDRAGIT® L as taught by Shimono et al. and to embed in the inner matrix layer a protein/peptide active ingredient, as taught by Watts et al. Shimono et al. demonstrates that microcapsules with this release profile need not be constructed with an inner matrix containing gelatin and can be made using chitosan without gelatin.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW